PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Global Intellectual Property
AstraZeneca
151 85 SÖDERTÄLJE

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Rule 71.1)

Applicant's or agent's file reference 100709-1 WO	Date of mailing *(day/month/year)* 30-09-2004
	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SE2003/000856	27-05-2003	30-05-2002

Applicant
AstraZeneca AB
et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in som Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the *PCT Applicant's Guide*.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, intentive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed invention is patentable or not" (see Also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the IPEA/	Authorized officer
Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. 08-667 72 88 Telex 17978 PATOREG-S	Christina Wall Telephone No. 08-782 25 00

Form PCT/IPEA/416 (January 2004)

PATENT COOPERATION TREATY

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CODE	DATE	NTD

ANKOM 11 OCT 2004 GIPS

DATA ENTERED

FINAL CHECK

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION See Form PCT/IPEA/416	
100709-1 WO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/SE 2003/000856	27.05.2003	30.05.2002

International Patent Classification (IPC) or national classification and IPC

C07D 209/30,403/12, 417/12, 413/12, A6131/405, 31/4178, 31/4196, 31/422,31/4709, 31/427, A61P 11/06, 11/00, 29/00

Applicant

AstraZeneca AB et al

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:

a. ☒ *(sent to the applicant and to the International Bureau)* a total of 1 sheets, as follows:

- ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
- ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.

b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))

_____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

- ☒ Box No. I Basis of the report
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
17.12.2003	23.09.2004
Name and mailing address of the IPEA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. +46 8 667 72 88	Authorized officer Eva Johansson/EÖ Telephone No. +46 8 782 25 00

Form PCT/IPEA/409 (cover sheet) (January 2004)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SE 2003/000856

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

☐ international search (under Rules 12.3 and 23.1(b))
☐ publication of the international application (under Rule 12.4)
☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

☐ the international application as originally filed/furnished

☒ the description:

pages 1-48 as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☒ the claims:

pages 49-52 as originally filed/furnished
pages* _____ as amended (together with any statement) under Article 19
pages* 53 received by this Authority on 27-07-2004
pages* _____ received by this Authority on _____

☐ the drawings:

pages _____ as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☐ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

☐ the description, pages _____
☐ the claims, Nos. _____
☐ the drawings, sheets/figs _____
☐ the sequence listing *(specify)*: _____
☐ any table(s) related to the sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 7 and 8

because:

☒ the said international application, or the said claims Nos. 7 and 8 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

See PCT Rule 67.1.(iv).: Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in the Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SE 2003/000856

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-6, 9	YES
	Claims		NO
Inventive step (IS)	Claims	1-6, 9	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-9	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

New amended claims 8 and 9 have been filed 2004-07-27.
The new claim 8 is the same as the earlier claim 8 and the structure formula in claim 9 has been corrected.

The earlier claim 10, which relates to an intermediate, is deleted. Claim 11 is deleted.

The following documents are cited in the search report:

The cited documents 1-12 assign to the earlier claim 10.

D1 STN International, File CAPLUS, CAPLUS accession no. 1977:535057, Document no. 87:135057 & JP,A2, 52039671

D2 STN International, File CAPLUS, CAPLUS accession no. 2001:338492, Document no. 134:353315 & WO, A1, 2001032621

D3 Tetrahedron Letters, Vol. 26, no. 15, 1985, page 1827-1830

D4 STN International, File CAPLUS, CAPLUS accession no. 1988:549279, Document no. 109:149279

D5 J. Org. Chem., Vol. 66, no. 7, 2001, page 2434-2441

D6 Tetrahedron Letters, Vol. 42, no. 6, 2001, page 1077-1080

D7 Tetrahedron Letters, Vol. 42, no. 31, 2001, page 5187-5189

D8 J. Org. Chem., Vol. 61, no. 5, 1996, page 1573-1577

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

D9 EP 530907

D10 WO 9516687

D11 WO 9419321

D12 EP 576347

D13 EP 1170594 A2

D14 GB 1356834 A

D15 STN International, File Chemcats, Chemcats acc. no. 2000:1027702

D16 STN International, File CAPLUS, CAPLUS acc. no. 1983:488557, doc. no. 99:88557

D1-D12 disclose compounds, which were earlier included in the scope of previous claim 10. The compounds are excluded from the claims.

The claimed invention relates to novel indole-derivatives as pharmaceutical compounds for treating respiratory disorders and a process for their preparation.

The cited documents D13-D16 represent the general state of the art.
The invention defined in claims 1-6 and 9 is not disclosed by any of these documents.
The cited prior art does not give any indication that would lead a person skilled in the art to the claimed novel indole-derivatives as pharmaceutical compounds for treating respiratory disorders. Therefore, the claimed invention is not obvious to a person skilled in the art.

Accordingly, the invention defined in claims 1-6 and 9 is novel and is considered to involve an inventive step. The invention is industrially applicable.

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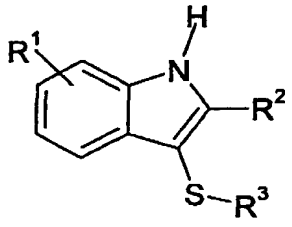
27-07-2004

8. A method of treating according to claim 7 wherein the disease is asthma or rhinitis.

9. A process for the preparation of a compound of formula (I) which comprises reaction of a compound of formula (II):



(II)

in which R^1, R^2 and R^3 are as defined in formula (I) or are protected derivatives thereof, with a compound of formula (A):

$L\text{-}CH_2CO_2R^{17}$ (A)

where R^{17} is an ester forming group and L is a leaving group in the presence of a base, and optionally thereafter in any order:

- removing any protecting group
- hydrolysing the ester group R^{17} to the corresponding acid
- forming a pharmaceutically acceptable salt.